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ABSTRACT

Since 1959, tissues from 70 former employees of the Los Alamos Scientific Laboratory with occupational exposures to plutonium have been examined following autopsy. Chemical analyses of selected tissues were performed to determine the amount of plutonium retained in the body at the time of death. Based upon the measured tissue concentrations of plutonium, extrapolations of total body burdens were made. Exposure in most cases was to inhaled plutonium oxide aerosols. Thirty-three of the measured cases had plutonium depositions in the tracheobronchial lymph nodes ranging from 0.1 to 4000 dis/min per gram of tissue (0.05 to 1800 pCi/g). The duration of exposures ranged from 4 to 30 years. Microscopic examination of representative sections of these lymph nodes revealed no abnormalities other than those which were directly attributable to the basic disease which caused the demise of the various persons in this study. The size distribution of plutonium particles in nodes from one case was determined by exposure of tissue sections to nuclear track film. The estimated mass median diameter of the particles was 0.3 μm and the distribution had a geometric standard deviation of 1.6 It is estimated that 95% of the individual particles had corresponding plutonium concentrations between 0.001 and 0.22 pCi.

* Work supported by the U. S. Atomic Energy Commission.

** Also affiliated with the Los Alamos Medical Center.

INTRODUCTION

A great deal of interest and concern has been generated regarding the effects of internally deposited alpha emitting radioisotopes on the human body. While animal data are abundant, the collection of human data has been rather meager and the extrapolation from animals to humans always results in some doubt as to its reliability. Tissue from 70 former employees of the Los Alamos Scientific Laboratory (LASL) who had potential occupational exposures to plutonium have had tissues removed for analysis after death. Histologic studies were made on most of these cases. Radiometric analyses were performed on these same tissues to determine the amount of plutonium, if any, retained at the time of death. From these data, whole body contents of plutonium were extrapolated and compared to in vivo estimates from urine analysis data and lung counting techniques.[1] This is part of the on-going program at LASL to improve the urine bioassay calculations on laboratory personnel currently working in the plutonium laboratories. Thirty-three of the cases analyzed chemically had tracheobronchial lymph node depositions of plutonium ranging from 0.1 to as high as 4000 dis/min per gram of tissue (0.05 to 1800 pCi/g). This paper reports the plutonium concentrations and pathological data on those cases where the tracheobronchial lymph nodes were examined at autopsy. In Case 7-138, in which the highest concentration of plutonium was observed (1800 pCi/g), attempts were made to estimate the size range of the plutonium particulates dispersed throughout the node.

METHODS

The whole lung and associated tracheobronchial lymph nodes, the liver, kidneys and a bone specimen (usually a vertebral wedge) are routinely taken at autopsy for radiometric analyses. Small samples were removed from these tissues and processed with other tissues of specific interest to the pathologist as part of the autopsy protocol. Histological slides of tracheobronchial lymph nodes were available for study in 14 of the above mentioned cases.

The tissues were weighed, muffled and the inorganic residue wet-ashed in nitric acid. The resulting salts were treated with hydrofluoric acid to solubilize any remaining plutonium ceramics and, after removing the excess fluorides, dissolved in nitric acid. Initially, an internal tracer of ^{236}Pu, more recently replaced by ^{242}Pu, was used to determine the chemical yield of the $^{239-240}Pu$ and ^{238}Pu. The plutonium was isolated by anion exchange and electrodeposited onto stainless steel disks. Alpha pulse height spectrometry was utilized to measure the 4.9 to 5.7 Mev Pu alpha energies.

In a few cases of suspected high levels of activity in the lymph nodes, the specimen was counted with a thin CsI-NaI x-ray detector for both the 17 kev x-ray emitted by the Pu and the 17 and 60 kev x-rays associated with ^{241}Am. This method has the advantage of being nondestructive and was used to obtain the relative activities in each of the 12 lymph nodes obtained from Case 7-138, an occupationally exposed worker with an estimated body burden of 33 nCi of ^{239}Pu based on urine assay.[2] (See Table 1). Two of the nodes containing the highest alpha activity were selected for

autoradiography. The formalin-fixed nodes were embedded in paraffin and cut into 6, 12 and 18 μm thick sections, mounted on standard microscope slides and stained. The slides were dipped into nuclear track photographic emulsion and the film allowed to expose for one week under standard nuclear track activity (N.T.A.) conditions. The slides were then developed and examined for the presence of alpha tracks. A typical star pattern resulting from this method of recording the presence of alpha active particulates is illustrated in Fig. 1. By counting the number of tracks in the emulsion associated with each star and by knowing the exposure time, the size of each alpha emitting particle can be calculated from the formula:[3]

$$d=\left(\frac{KC}{t}\right)^{1/3} \qquad (1)$$

where C=the number of tracks in the emulsion from particle of diameter d microns, assuming 50% geometry

t=autoradiograph exposure time, and

K=constant = $6.32\text{X}10^{-12}\left(\frac{M}{\rho\lambda f}\right)$ = 2.76 for $^{239}PuO_2$

M=molecular weight of compound = 271 for $^{239}PuO_2$

ρ=density of compound = 11.46 g/cm^3

λ=decay constant of the alpha emitter, and

f=number of radioactive atoms per molecule of compound.

The alpha tracks were assumed to originate from $^{239}PuO_2$ particles. A seven day exposure and a three track star permit the detection of a Pu particle of 0.09 μm in diameter (0.0002 pCi Pu). The tissue sections used in this study were also examined histologically for evidence of abnormalities resulting from the alpha radiation.

RESULTS

A. Observed Alpha Radiation Effects on Tracheobronchial Lymph Nodes.

Selected information on the 14 autopsy cases in which the tracheobronchial lymph nodes were examined both histologically and chemically is shown in Table 2. The years since the first potential exposure is represented by the time from the date of hiring at LASL to death. It was assumed the exposure incidents were inhalation exposures that occurred during the early years of the laboratory operation (1945-1955) before improved industrial hygiene and health physics requirements reduced significantly the air levels of plutonium in the laboratories and the workers were provided with more efficient personal respiratory protection.

Microscopic examination of the stained thin sections of lymph node revealed no abnormalities other than what would be expected from the individual disease processes that caused the demise of the various cases in this study. Many of the nodes appeared to contain normal activity, such as hyperplasia, as in the case of pneumonia, and tumor metastasis, in the case of cancer. The pulmonary nodes of persons dying from trauma were pathologically unremarkable.

B. $^{239}PuO_2$ Particle Size Distribution in Lymph Node.

Because of the relatively high levels of deposition observed in the lymph nodes of Case 7-138, a metal fabrication technician with 26 years of employment at LASL, it was deemed feasible to attempt the measurement of the alpha emitting particle size distribution using the autoradiographic techniques developed by Leary.[3]

Table 3 lists the calculated relationships between the number of alpha tracks radiating outward from a particle to the $^{239}PuO_2$ particle diameter and the amount of ^{239}Pu present in fCi per particle. These data are corrected for the mean contribution of ^{241}Am that is suspected in the nodes. The frequency distribution of $^{239}PuO_2$ particle sizes, as determined by the manual counting of the alpha tracks associated with 1215 stars observed in lymph node No. 6 are shown in Table 4. These data were assumed to be log-normally distributed and the log-probability plot of these data is shown in Fig. 2. Because the distribution of count diameters is a log-normal function, a mass diameter plot can be calculated from these data using the Hatch-Choate equations.[4] The alpha emission rate is directly proportional to the mass of $^{239}PuO_2$ present in the particles and, therefore, the mass diameter plot also represents the distribution of particles by activity. The frequency of the various size $^{239}PuO_2$ particles in this lymph node as projected from the least squares fit of the midpoints of the frequency distribution of particle sizes in Fig. 2 is tabulated in Table 5. Data on the size distribution of Pu particulates in two other nodes, Nos. 8 and 11, gave similar results.

The size frequency distribution of Pu particulates in the tracheobronchial lymph nodes of Case 7-138 appeared to be similar to the size distribution of Pu aerosols sampled and measured during Pu fluorination and reduction operations in the facility in which this employee worked.[5,6] (See Table 6). From the tabulation of Pu aerosol sizes and the estimated Pu activity in the entire node (660 pCi) the number of Pu particles of various diameters

were calculated. (See Table 5). The parameters associated with the logarithmic normal distribution indicate that 95% of the alpha active particles in this lymph node have corresponding Pu activities between 0.001 pCi and 0.22 pCi.

SUMMARY

Microscopic examination of lymph node tissue from occupationally exposed workers has revealed no abnormalities other than those directly attributable to the basic disease that caused the death of the various persons in this study.

The distribution of $^{239}PuO_2$ particles in one tracheobronchial lymph node was determined to have a mass median diameter of 0.3 μm with a geometric standard deviation of 1.6. Ninety-five percent of the particles in the node were estimated to have a ^{239}Pu concentration less than 0.22 pCi.

Studies on the distribution and effects of Pu particulates in lymphatic tissue are continuing.

Note: The authors express their appreciation to Harold Ide for the x-ray measurement of ^{239}Pu and ^{241}Am concentrations in the lymph nodes, and to Bernard C. Eutsler for counting the alpha tracks associated with each star.

REFERENCES

1. J. F. McInroy, J. J. Johnson, E. E. Campbell, W. D. Moss, and H. F. Schulte, "Plutonium Concentrations in Tissue of Occupationally Exposed Workers," Los Alamos Scientific Laboratory Report, LA-4876 (1974).

2. J. N. P. Lawrence, Health Division, Los Alamos Scientific Laboratory, Los Alamos, New Mexico. Personal communication.

3. J. A. Leary, "Particle-Size Determination in Radioactive Aerosols by Radioautograph, Analytical Chemistry, 23:850-853 (1951).

4. T. Hatch, and S. P. Choate, "Statistical Description of the Size Properties of Non-Uniform Particulate Substances," J. Franklin Inst. 207, 369 (1929).

5. C. R. Richmond, Oak Ridge National Laboratories, Oak Ridge, Tennessee. Personal communication.

6. W. D. Moss, E. C. Hyatt, and H. F. Schulte, "Particle Size Studies on Plutonium Aerosols," Health Physics, 5:212-218 (1961).

Table 1

CONCENTRATION OF PLUTONIUM AND AMERICIUM IN THE TRACHEOBRONCHIAL LYMPH NODES OF A PLUTONIUM WORKER

Node No.	Weight mg	Estimated Isotope Concentration* pCi per node ^{239}Pu	pCi per node ^{241}Am	pCi per Gram Tissue ^{239}Pu	pCi per Gram Tissue ^{241}Am	Pu/Am
1	589	274	29	465	149	9.5
2	131	26	4	198	30	6.6
3	159	ND	ND	ND	ND	---
4	275	74	10	269	36	7.4
5	448	151	28	337	62	5.4
6	625	659	77	1054	123	8.5
7	500	483	44	966	88	11.0
8	108	119	3	1102	28	39.3**
9	114	39	7	342	61	5.6
10	180	182	12	1011	67	15.1
11	181	327	26	1806	144	12.5
12	433	401	39	926	90	10.3
			Mean	770	80	9.2
			±1S.D.	493	43	3.1

* Based on 17 and 60 kev X-radiation measurement

**Not included in calculated mean of data

ND = not detectable

Table 2

CONCENTRATION OF ^{239}Pu IN TRACHEOBRONCHIAL LYMPH NODES OF OCCUPATIONALLY EXPOSED WORKERS

Case No.	Occupation	Cause of Death	Year of Death	Age at Death	Years since 1st Exposure*	Alpha Activity in TBLN, pCi/g
7-138	Metal Fabrication Technician	Crushed Chest	1973	47	26	770
5-138	Chemist	Living***	1971***	50***	27	254
2-004	Health Physics Monitor	Cancer (lung)	1961	68	12	29
5-114	Chem. Tech.	Sroke	1970	49	21	6.3
7-084	Pipefitter	Cancer (lung)	1972	58	23	1.8
7-004	Accountant	Carcinoma 'colon)	1971	76	24	0.24
1-150	Plumber	Cardiac	1961	51	8	0.23
5-024	Physicist	Heart Attack	1969	43	5	0.21
7-076	Maint. Mech.	Rup'td Aorta	1972	72	24	0.18
3-142	Engineer	Cardiac Arrest	1969	48	14	0.11
7-016	Machinist	Heart Attack	1971	62	26	0.09
3-108	Technician	Pneumonia	1968	69	26	0.09
3-086	Technician	Diabetes	1968	34	15	0.05
7-028	Design Eng.	Heart Disease	1971	60	28	0.05

* Years from time of hire to death

** TBLN = tracheobronchial lymph node

***Biopsy tissue taken in 1971

Table 3

ALPHA TRACKS ASSOCIATED WITH $^{239}PuO_2$ PARTICLE DIAMETER AND CONCENTRATION IN PARTICLE

Number of Tracks	Plutonium Particle Diameter, μm	Plutonium Concentration per Particle, fCi
5	0.11	0.4
10	0.14	0.9
20	0.18	1.8
30	0.20	2.7
40	0.22	3.6
50	0.24	4.5
100	0.30	8.9
200	0.38	17.9
500	0.52	44.7
1000	0.65	89.4

Table 4

FREQUENCY DISTRIBUTION OF PLUTONIUM PARTICLES FROM STARS OBSERVED IN TRACHEOBRONCHIAL LYMPH NODE #6, 7-138, (0.66 nCi)

Plutonium Particle Diameter μm	Frequency	Cumulative Percent
0.11	92	7.5
0.14	141	19.2
0.18	146	31.2
0.20	147	43.1
0.22	125	53.6
0.24	206	70.5
0.30	199	86.9
0.38	92	94.5
0.52	52	98.8
0.65	15	100.0

Table 5

FREQUENCY OF $^{239}PuO_2$ PARTICLES IN TRACHEOBRONCHIAL LYMPH NODE #6, 7-138

Diameter, μm	Midpoint	Cumulative Fraction	Incremental Fraction	Activity, pCi/particle	Activity, pCi/node	Particles per node
	0.1		0.12	0.0003	79	2.6×10^5
0.2		0.12				
	0.3		0.58	0.009	382	4.2×10^4
0.4		0.70				
	0.5		0.23	0.041	151	3.7×10^4
0.6		0.93				
	0.7		0.056	0.11	37	3.4×10^2
0.8		0.986				
	0.9		0.011	0.24	7	2.9×10^1
1.0		0.997				
	1.1		0.002	0.43	1	2.0×10^0
1.2		0.999				
					Total	3.4×10^5

Table 6

DATA ON AVERAGE PARTICLE COUNT MEDIAN AND MASS MEDIAN DIAMETERS MEASURED IN METAL PREPARATION AREA AND METAL FABRICATION AREA, LOS ALAMOS SCIENTIFIC LABORATORY[6]

Operation in Area	Count Median Diameter, μm	Geometric Standard Deviation, σ_g	Mass Median Diameter, μm
Fluorination of nitrate	0.26	1.5	0.45
Reduction to metal	0.17	1.6	0.32
Lathe operation	0.19	1.4	0.28

Fig. 1. Tracheobronchial lymph node tissue section showing alpha tracks radiating out from an an alpha active particle in a typical "star" pattern.

McInroy, FIG. 1.

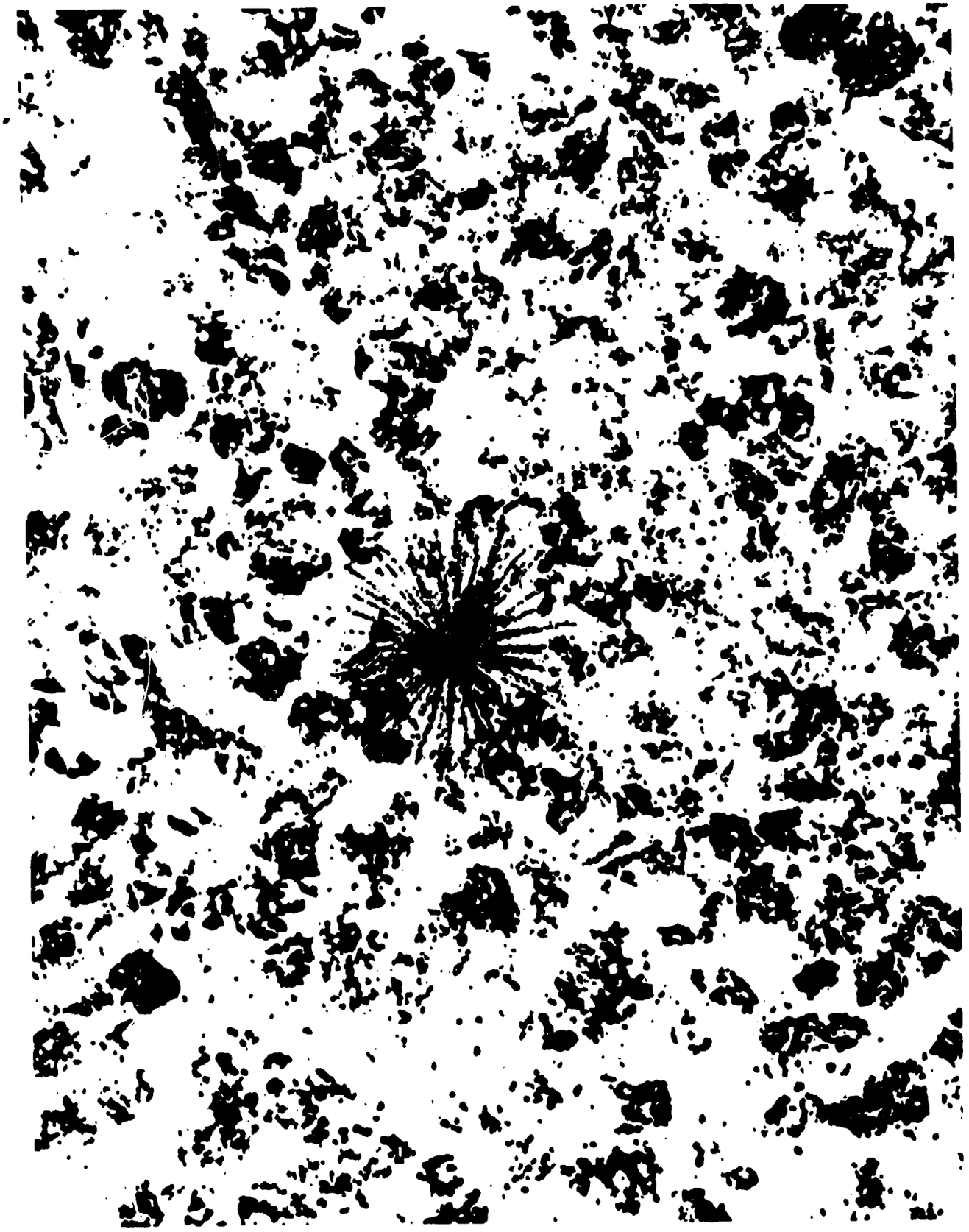
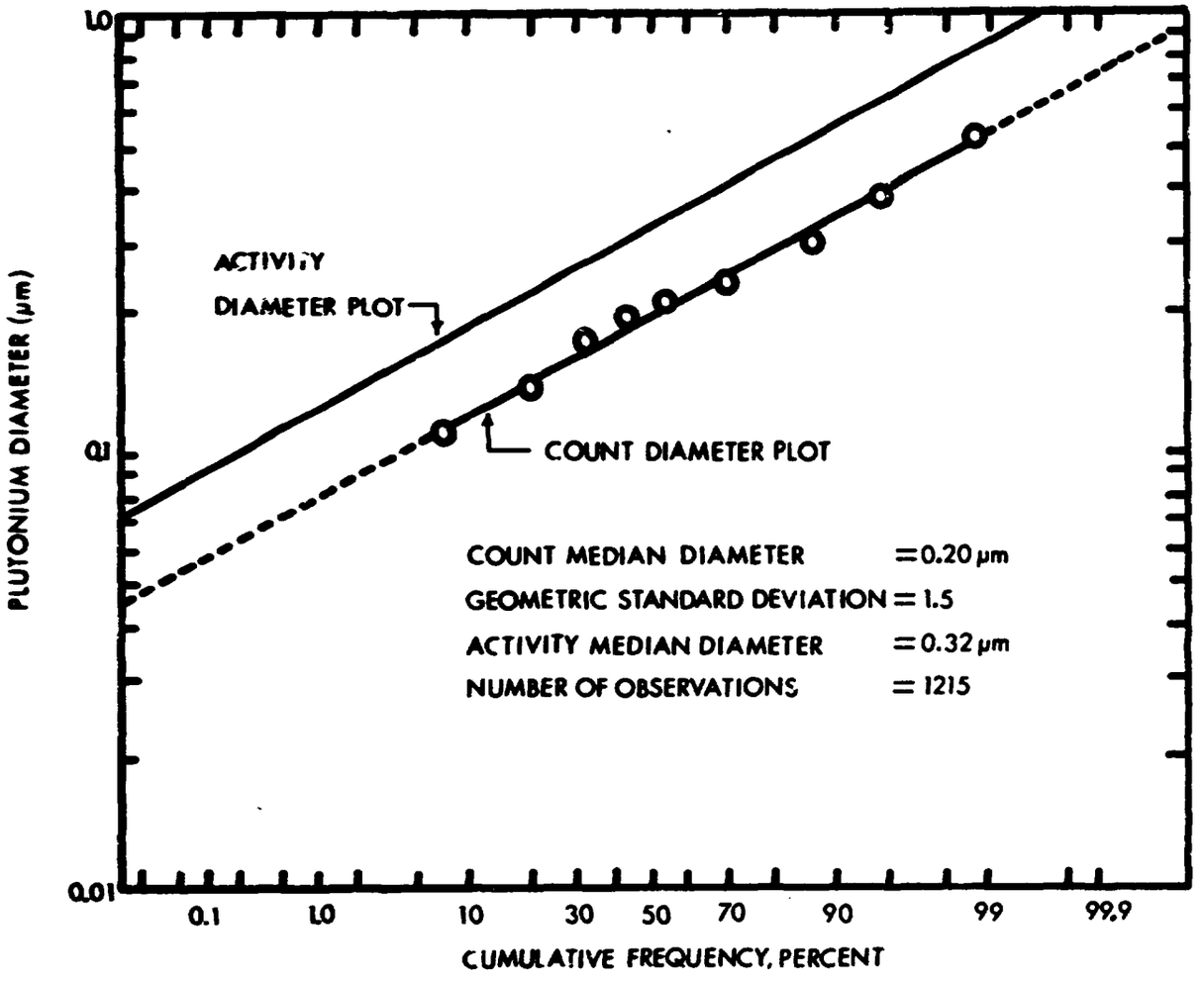


Fig. 2. Log-normal cumulative frequency plot of $^{239}PuO_2$ particles in tracheobronchial lymph node.


1.0
0.1
0.01
PLUTONIUM DIAMETER (μm)
ACTIVITY
DIAMETER PLOT
COUNT DIAMETER PLOT
COUNT MEDIAN DIAMETER =0.20 μm
GEOMETRIC STANDARD DEVIATION = 1.5
ACTIVITY MEDIAN DIAMETER =0.32 μm
NUMBER OF OBSERVATIONS = 1215
0.1
1.0
10
30
50
70
90
99
99.9
CUMULATIVE FREQUENCY, PERCENT